INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP03/16600

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished.

☒ the description:
pages 1-24 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:
Nos. 2, 3, 6-17, 19 as originally filed/furnished
Nos.* _____ as amended (together with any statement) under Article 19
Nos.* 1, 5, 18, 20, 21 received by this Authority on September 27, 2004
Nos.* _____ received by this Authority on _____

☒ the drawings:
~~sheets~~/figs 1-8 as originally filed/furnished
sheets/figs* _____ received by this Authority on _____
sheets/figs* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☒ the claims, Nos. 4

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded".*

Translation of PCT Article 34 Amendment

CLAIMS

1.(Amended) A marker protein for diagnosing liver disease selected from a protein which is a human fibrinogen α-E chain decomposition product and has a molecular weight of 5,900 (5.9 kDa protein), a protein which is an apolipoprotein AII decomposition product and has a molecular weight of 7,800 (7.8 kDa protein) and variants of these proteins which have the same function as that of the proteins as a marker protein for diagnosing liver disease.

2. A marker protein for diagnosing liver disease according to claim 1, wherein the 5.9 kDa protein is a protein having the amino acid sequence shown as SEQ ID NO: 1 in the sequence listing, and the variant thereof is a protein having 90% or more homology with said amino acid sequence or a protein having an amino acid sequence formed by deletion, substitution or addition of one or more amino acid residues in the amino acid sequence shown as SEQ ID NO: 1.

3. A marker protein for diagnosing liver disease according to claim 1, wherein the 7.8 kDa protein is a protein having the amino acid sequence shown as SEQ ID NO: 2 in the sequence listing, and the variant thereof is a protein having 90% or more homology with said amino acid sequence or a protein having an amino acid sequence formed by deletion, substitution or addition of one or more amino acid residues in the amino acid

sequence shown as SEQ ID NO: 2.

4.(Deleted)

5.(Amended) A marker protein for diagnosing liver disease according to any one of claims 1 to 3, which is for diagnosing a liver disease caused by drinking.

6. A marker protein for diagnosing liver disease according to claim 5, which is for diagnosing an alcoholic liver trouble or alcohol dependence.

7. A method for diagnosing the probability of the onset of a liver disease, the liver disease or the prognosis of the liver disease by detecting or quantifying the marker protein for diagnosing liver disease according to any one of claims 1 to 6 in a sample obtained from a patient who is suspected to have the liver disease.

8. A diagnosis method according to claim 7, wherein the liver disease is a liver disease caused by drinking.

9. A diagnosis method according to claim 8,

wherein the liver disease is an alcoholic liver trouble or alcohol dependence.

10. A diagnosis method according to any one of claims 7 to 9, wherein the detection or quantification of the marker protein for diagnosing liver disease in the sample is carried out by mass spectrometry.

11. A diagnosis method according to claim 10, wherein the diagnosis is carried out by analyzing the pattern of a spectrum obtained with a mass spectrometer.

12. A diagnosis method according to claim 10 or 11, wherein the mass spectrometry is carried out with a laser desorption/ionization-time of flight-mass spectrometer (LDI-TOF MS).

13. A diagnosis method according to claim 12, wherein the laser desorption/ionization-time of flight-mass spectrometer is a surface enhanced laser desorption/ionization-time of flight-mass spectrometer (SELDI-TOF MS).

14. A diagnosis method according to any one of claims 7 to 9, wherein the detection or quantification of the marker protein for diagnosing liver disease in the sample is carried out by an immunoassay method using an antibody against said protein.

15. A diagnosis method according to claim 14, wherein the immunoassay method is an enzyme immunoassay method (EIA method), an immunoturbidimetry method (TIA method), a latex immuno-agglutination method (LATEX

method), an electrochemiluminescence method or a fluorescence method.

16. A diagnosis method according to claim 15, wherein the immunoassay method is an enzyme immunoassay method (EIA method).

17. A protein having the amino acid sequence shown as SEQ ID NO: 1 in the sequence listing, or its variant having the same function as that of said protein as a marker protein for diagnosing liver disease, said variant being a protein having 90% or more homology with said amino acid sequence or a protein having an amino acid sequence formed by deletion, substitution or addition of one or more amino acid residues in the amino acid sequence shown as SEQ ID NO: 1.

18.(Amended) A protein having the amino acid sequence shown as SEQ ID NO: 2 in the sequence listing.

19. A method for measuring a protein or its variant according to claim 17 or 18, or a protein which is apolipoprotein AI and has a molecular weight of

28,000 or its variant having the same function as that of this protein as a marker protein for diagnosing liver disease, by an immunoassay method by the use of an antibody against each of the proteins or the variants.

20.(Amended) A method according to claim 19, wherein the immunoassay method is an enzyme immunoassay method (EIA method), an immunoturbidimetry method (TIA method), a latex immuno-agglutination method (LATEX method), an electrochemiluminescence method or a fluorescence method.

21.(Amended) A method according to claim 20, wherein the immunoassay method is an enzyme immunoassay method (EIA method).